REMARKS

The office action of May 15, 2008 has been carefully reviewed. Claims 1-5, 8-13, 16-69 are pending. Claims 1-5, 11, 16-23, 25-69 have been amended. Claims 8-10, 12, 13, and 24 have been canceled.

SPECIFICATION

A. The Examiner objected to the manner in which several words should be written in the specification. Applicants have amended the specification to address these issues. The Examiner further stated that ""Diamine" was misspelled in the claim." Applicants contend that the "Diamine" is not found in the claims. If the Examiner maintains this objection, Applicants respectfully request that specifically points out the claim number containing this misspelling so it can be properly amended.

B. The Examiner previously alleged that equations (1)-(4) on pages 51, 55, and 58 of the specification of the subject application contain typographical errors. These equations have been amended in the specification such that they are now correct.

C. The Applicants wish to point out to the Examiner that the specification defines two distinct terms, $IAR_{\lambda,j}$ and $IA_{\lambda,j}$. These two terms are correctly defined in the specification in the amended paragraphs [00165] and [00170], respectively. The "R" designates that the term is a ratio between the selected infrared wavelength band and the reference band. The absence of the "R" signifies that a term is not a ratio, but rather the mean-centered integrated absorbance. Accordingly, the Examiner's objection to Equations (2) and (3) is rendered moot by the present amendments and explanation.

D. Applicants submit that a practitioner of ordinary skill in the art would not consider the use of units of wavenumbers (cm^{-1}) or wavelengths (μm or microns) to be cumbersome or inconvenient and would be routinely accustomed to either. Applicants reminds the Examiner of MPEP section 608.01(g) which states: "An applicant is ordinarily permitted to use his or her own terminology, as long as it can be understood. Necessary grammatical corrections, however, should be required by the examiner, but it must be remembered that an examination is not made for the purpose of securing grammatical perfection." Applicants

contend that units utilized in the specification are the most commonly used units in this art and are easily understood.

E. The Examiner pointed out a typographical error in paragraph [00155]; Applicants have amended the specification to correct this error.

DOUBLE-PATENTING

A. Applicants have canceled claims 8-10, 12, and 13 to address the Examiner's objections.

B. The Examiner has provisionally rejected instant claims 1-5, 8-13 and 16-69 on the ground of nonstatutory double-patenting over claims 1-24 of U.S. Patent 7,288,768 (the '768 patent), contending that the subject matter claimed in the instant application is not patentably distinct from the '768 patent.

Applicants request that the Examiner hold this rejection in abeyance until allowable subject matter is indicated.

CLAIM OBJECTIONS

A. The Examiner has requested that claims 8, 16 and 58 recite both measurement units of wavelengths (μm or microns) and wavenumbers (cm^{-1}); accordingly, claims 16 and 58 were amended. Claim 8 was canceled.

B. The Examiner has objected to claims' 28 and 57 recitation of the term "thickness" of an absorbance band; accordingly, Applicants amended the claims 28 and 57 to recite the term "bandwidth".

C. Applicants have amended claims 35 and 36 to correct the typographical error pointed out by the Examiner.

CLAIM REJECTIONS BASED ON §112, FIRST PARAGRAPH

The Examiner rejected claims 19-22 under 35 U.S.C. §112, first paragraph alleging that the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 19-22 were amended to include the phrase "measured using methods other than IR absorption" as supported by the definition in the specification at paragraphs [00158], [00164], [00165] and [00170]. Applicants acknowledge that the previous amendment to the claims or specification did not completely address errors associated with equations (1)-(4). Applicants have amended these equations accordingly. Furthermore, the claims were amended to properly align the equations (1)-(4) with obtaining the calibration coefficients.

CLAIM REJECTIONS BASED ON §112, SECOND PARAGRAPH

The Examiner rejected claims 2, 18-22 28-69 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim subject matter which Applicants regard as the invention. Each pending claim was either amended or cancelled to address the Examiner's rejections.

CLAIM REJECTIONS BASED ON §102

A. The Rejections of Claims 1-5, 8-9, 11-13, and 16-27

In the official action, the Examiner rejected claims 1-5, 8-9, 11-13, and 16-27 under 35 U.S.C. §102(e) as being anticipated by U.S. Pat. No. 6,484,044 to Lillenfeld-Toal (the '044 Patent).

Applicants respectfully direct the Examiner to Claim 1 which is included below, as amended, for the Examiner's convenience:

1. A method of measuring an amount of an organic substance contained within a biological sample utilizing a detection system, comprising:

(a) transmitting incoherent infrared radiation through a sample;

(b) detecting the intensity of the transmitted radiation with an optical sensor;

(c) generating an electrical signal in response thereto;

(d) receiving the electrical signal with a signal processor configured to process the electrical signal with a quantification algorithm; and

(e) processing the electrical to provide a measure of the amount of the organic substance contained within the sample; wherein,

(i) one or more reference samples, each containing a known amount of the organic substance, are measured thereby calibrating the detection system,

(ii) the biological sample and the reference sample each have an infrared absorption spectrum which includes a set of n selected wavelength regions,

(iii) up to n-1 of the wavelength regions each substantially correspond to an absorption band of the organic substance, and

(iv) at least one of the wavelength regions substantially corresponds to a reference absorption band.

Applicants respectfully direct the Examiner's attention to the fact that one element of claim 1 is "transmitting incoherent infrared radiation through a sample." The '044 Patent is devoid of any teaching regarding transmitting incoherent infrared radiation through a sample. Since the '044 Patent fails to teach each and every element of claim 1, Applicants' request that this rejection be withdrawn.

Claims 2-5, 11, and 16 contain every element of claim 1. Accordingly, the '044 Patent fails to teach each and every element of claims 2-5, 11, and 16 and Applicants request that these rejections be withdrawn.

Applicants respectfully direct the Examiner to Claim 17 which is included below, as amended, for the Examiner's convenience:

17. A method of measuring a concentration of an organic substance contained within a biological fluid, comprising:

(1) calibrating a detection system by the steps of:

(a) detecting, with an optical sensor, the transmittance of n selected wavelength bands of incoherent infrared radiation through a reference fluid,

(b) generating an electrical signal in response thereto,

(c) receiving the electrical signal with a signal processor configured to process the electrical signal with a mathematical model, and

(d) processing the electrical signal to calibrate the detection system;

(2) utilizing the detection system to give a measure the concentration of the organic substance contained within the biological fluid.

Applicants respectfully direct the Examiner's attention to the fact that one element of claim 17 is "detecting, with an optical sensor, the transmittance of n selected wavelength bands of incoherent infrared radiation through a reference fluid." The '044 Patent is devoid of any teaching regarding detecting, with an optical sensor, the transmittance of n selected wavelength bands of incoherent infrared radiation through a reference fluid. Since the '044 Patent fails to teach each and every element of claim 17, Applicants' request that this rejection be withdrawn.

Claims 18-22 contain every element of claim 17. Accordingly, the '044 Patent fails to teach each and every element of claims 18-22 and Applicants request that these rejections be withdrawn.

Applicants respectfully direct the Examiner to Claim 23 which is included below, as amended, for the Examiner's convenience:

> 23. A method of measuring an amount of an organic substance contained within a biological sample having an infrared absorption spectrum which includes a set of n absorption regions, wherein up to n-1 of the absorption regions are absorbed by the organic substance and at least one of the absorption regions, a reference absorption region, does not correspond to the absorption regions of the organic substance, comprising:
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> (a) illuminating the biological sample with infrared electromagnetic radiation, wherein the infrared electromagnetic radiation is transmitted through the sample;
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> (b) selecting n-1 or less absorption bands from the absorption regions absorbed by the organic substance;
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> (c) selecting 1 or more reference wavelength bands from the absorption regions in which the organic substance does not absorb;
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> (d) optically detecting the intensity of the transmitted electromagnetic radiation at the n absorption bands;
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> (e) generating one or more electrical signals in response to detecting the intensity of the n absorption bands;
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> (f) receiving the electrical signals with a signal processor configured to process the electrical signals with a quantification algorithm; and
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> (g) processing the electrical signals with the quantification algorithm so as to provide a measurement of the amount of the organic substance contained within the biological sample.

Applicants respectfully direct the Examiner's attention to the fact that one element of claim 23 is "optically detecting the intensity of transmitted electromagnetic radiation." The '044 Patent is devoid of any teaching regarding optically detecting the intensity of transmitted electromagnetic radiation. Since the '044 Patent fails to teach each and every element of claim 23, Applicants' request that this rejection be withdrawn.

Claim 25 contains every element of claim 23. Accordingly, the '044 Patent fails to teach each and every element of claim 25 and Applicants request that this rejection be withdrawn.

Applicants respectfully direct the Examiner to Claim 26 which is included below, as amended, for the Examiner's convenience:

> 26. A method of measuring an amount of an organic substance contained within a sample, the organic substance having an infrared absorption spectrum which includes a set (n) of wavelength regions, wherein up to n-1 of the wavelength regions each substantially correspond to an absorption band of the organic substance and at least one of the wavelength regions corresponds to a reference absorption band, comprising:
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> (a) calibrating a detection system with a reference sample;
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> (b) illuminating the sample with infrared electromagnetic radiation;
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> (c) filtering the electromagnetic radiation such that only radiation which corresponds to the n wavelength regions reaches a detector;
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> (d) detecting with the detector the intensity of the transmitted radiation.

Applicants respectfully direct the Examiner's attention to the fact that one element of claim 26 is "optically detecting with the detection system the intensity of the transmitted radiation." The '044 Patent is devoid of any teaching regarding optically detecting with the detection system the intensity of the transmitted radiation. Since the '044 Patent fails to teach each and every element of claim 26, Applicants' request that this rejection be withdrawn.

Applicants respectfully direct the Examiner to Claim 27 which is included below, as amended, for the Examiner's convenience:

> 27. A method of measuring an amount of an organic substance contained within a biological sample, the organic substance having an infrared absorption spectrum which includes a set (n) of wavelength regions, wherein up to n-1 of the wavelength regions substantially correspond to an absorption band of the organic substance and at least one of the wavelength regions corresponds to a reference wavelength band, comprising:
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> (a) calibrating a detection system with a set of reference samples;
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> (b) illuminating the biological sample with infrared electromagnetic radiation, wherein the infrared electromagnetic radiation includes (i) one or more discrete wavelength bands selected by filtering the electromagnetic radiation to correspond with the wavelength absorption bands of the organic substance contained within the biological sample and (ii) one or more discrete reference wavelength bands selected by filtering the electromagnetic radiation to correspond with a wavelength region not substantially absorbed by the organic substance contained within the biological sample;
>
> (c) optically detecting with the detection system the intensity of the infrared electromagnetic radiation transmitted through the biological sample; and
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> (d) processing with a mathematical model the intensity of transmitted infrared electromagnetic radiation of the discrete absorption bands corresponding to the organic substance absorption bands and the reference absorption bands.

Applicants respectfully direct the Examiner's attention to the fact that one element of claim 27 is "optically detecting with the detection system the intensity of ~~said~~ the infrared electromagnetic radiation transmitted through the biological sample." The '044 Patent is devoid of any teaching regarding optically detecting with the detection system the intensity of the infrared electromagnetic radiation transmitted through the biological sample. Since the '044 Patent fails to teach each and every element of claim 27, Applicants' request that this rejection be withdrawn.

CLAIM REJECTIONS BASED ON §103

12. The Examiner rejected claim 10 under 35 U.S.C. 103(a) as being unpatentable over Lillenfeld-Toal as evidenced by Peralta et al. The Applicants have canceled claim 10.

13. The Examiner has rejected Claims 28-51 and 56-69 under 35 U.S.C. 103(a) as being unpatentable over anyone of Heise et al. (Appl. Spear., 1994) (Heise), Bhandare et al. (Appl. Spear., 1994) (Bhandare), Budinova et al. (Appl. Spectr., 1997) (Budinova), or Vonach et al. (Appl. Spectr., 1998) (Vonach) in view of Purdy et al. (US 5,460,177), the '177 Patent.

The Examiner has stated that all references disclose a method of measuring a glucose level within a biological sample using mid-infrared spectroscopy by measuring a set of wavelength regions, in which glucose absorbs in mid-IR range: 1200-950 cm^{-1} (see e.g. Heise, page 88, left column) by obtaining a sample of a biological fluid, passing an incident signal of indicated wavelength through the sample, detecting a post-absorbance signals and calculating glucose concentration from said post-absorbance signal.

Applicants respectfully direct the Examiner to claim 28 and claim 57 which are included below, as amended, for the Examiner's convenience:

28. A method for determining a patient glucose level, comprising:

(1) obtaining a sample of cell-free blood-based body fluid in a sample container having a pre-defined measurement path;

(2) passing infrared radiation through the sample and sample container over the pre-defined measurement path to an optical detector, wherein the optical detector measures the intensity of radiation at less than 10 discrete wavelength bands, wherein:

(a) at least one of the wavelength bands corresponds to an absorption band of glucose,

(b) at least one of the wavelength bands does not correspond to an absorption band of glucose,

(c) each wavelength band has bandwidth of at least 140 nm, and

(d) the infrared radiation is modulated;

(3) optically detecting the infrared radiation using the optical detector;

(4) generating one or more electrical signals in response to detecting the infrared radiation; and

(5) calculating the patient glucose level by utilizing a calibration curve established with a series of samples with known glucose concentrations.

57. A method for determining a patient glucose level, comprising:

(1) calibrating a detector;

(2) obtaining a sample of a biological fluid in a sample container having a path of defined path length for the transmission of infrared radiation;

(3) transmitting modulated mid infrared radiation through the sample such that the infrared radiation is absorbed by glucose in the sample;

(4) detecting, with an optical sensor configured to detect modulated radiation, radiation corresponding to at least two glucose absorbance bands each having a bandwidth of at least 140 nm and radiation corresponding to at least one reference band and generating an electrical signal in response to detecting the modulated radiation, wherein the optical sensor uses spectral filtering channels;

(5) receiving the electrical signal with a signal processor configured to process the electrical signal with a quantification algorithm; and

(6) processing the electrical signal with the quantification algorithm, thereby providing a measurement of glucose contained within the sample.

Applicants respectfully direct the Examiner's attention to the fact that claim 28 recites the following: "passing infrared radiation through the sample and sample container over the pre-defined measurement path to an optical detector, wherein the optical detector measures the intensity of radiation at less than 10 discrete wavelength bands." Furthermore, an element of claim 57 is "wherein the optical sensor uses spectral filtering channels." Applicants submit that none of the references cited by the examiner teach or suggest either of these elements. In the contrary, each discloses methods utilizing FTIR spectrometers to obtain an entire spectrum of a sample. The Examiner stated:

> "All references disclose detecting glucose at specific wavelengths: "for glucose, the best predicting results were achieved within the rather narrow spectral range of 1200 to 950 cm^{-1}, where the most intensive absorption bands of aqueous glucose exist" (Heise, page 88, left column); Budinova discloses the following wave-numbers for glucose, which slightly differ from the ones recited in the claims: 1035, 1078, 1104 and 1148 cm^{-1} with the full range of 1185-950 cm^{-1}; Vonach indicates that "the spectral change [upon adding glucose] is in accordance with the glucose absorption with its maxima at 1038 and 1080 cm^{-1}" (page 821, left column).

However, the Examiner has failed to recognize that in each of the cited references, the disclosure is directed at analyzing FTIR spectra. An FTIR spectrum and the element of "the optical detector measures the intensity of radiation at less than 10 discrete

wavelength bands" are distinct. Similarly, An FTIR spectrum and the element of "the optical sensor uses spectral filtering channels" are distinct. Applicants agree with the Examiner that the absorption spectrum of glucose in the mid-infrared region is well-known in the art; however, the art cited by the Examiner fails to teach or suggest each element of claim 28 or 57.

Applicants point out that each of the cited references utilize FTIR (Fourier-Transform Infrared) spectroscopy. Heise (line 3 of the Abstract), Bhandare (paragraph 1 of Experimental), Vonach (line 1, Abstract) and Budinova (paragraph 3, introduction) each disclose the use of FTIR. Applicants submit that FTIR is patentably distinct from any element within claim 28 or 57. Heise distinguishes FTIR from "simple" transmission spectroscopy by stating, "[t]hese complications can be reduced with the use of near-infrared spectroscopy with simple transmittance experiments, for which cell pathlengths of millimeters are needed, so that the adsorbed layers play an extremely minor part in the absorbances measured." This excerpt, taken from the Conclusions, 2nd paragraph, is contrasting a "simple" transmittance experiment from an experiment utilizing Fourier transform mathematics and interferometer based optics. In this statement, Heise is implying that simple transmittance measurements are impossible with mid infrared radiation, however, near-infrared radiation can be used. Therefore, Heise is teaching away from matter claimed in claim 28 and 57 which do not describe the use of FTIR or near-infrared radiation. Similarly Budinova distinguishes a "simple transmittance" measurement from an FTIR measurement . Applicants respectfully refer Examiner to paragraph 2 and 3 of the Introduction on page 631 which is included below for the Examiner's convenience:

> The mid-IR region is useful in the invasive method of blood component determination by the attenuated total reflectance (ATR) technique[1-9] but simple transmittance measurements of liquid blood or blood serum are impossible in the mid-IR because of the presence of water in the matrix. ATR experiments are performed by employing ZnSe crystal-based flow cells; this approach, however, is associated with some shortcomings, such as the
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> adsorption of proteins on the crystal, which requires the cell to be demounted and the crystal to be polished frequently.
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> In the present work, the ATR technique was avoided; instead, the feasibility was examined of employing Fourier transform infrared (FT-IR) spectroscopy in the mid-IR region for determining glucose and cholesterol in whole blood and blood serum samples trapped on a polyethylene carrier and then dried.

Applicants point out that Budinova also teaches away from utilizing simple transmittance measurements of liquid blood or blood serum utilizing mid-IR. Examiner will

notice that Budinova states that "simple transmittance measurements of liquid blood or blood serum are impossible in the mid-IR because of the presence of water in the matrix." The Examiner will also appreciate that an element of both claim 28 and claim 57 is a biological fluid. In conclusion, Budinova teaches away from utilizing transmittance on biological fluids.

The disclosure of Bhandare does not teach a method for analyzing a sample containing glucose, but rather, Bhandare merely compares several different techniques for analyzing FTIR spectrum. Accordingly, it does not teach or suggest every element of claim 28 or 57 and has little or no relevance to claims which are not directed at FTIR spectroscopy. Claims 28 and 57 do not include a step incorporating an FTIR spectrometer. Furthermore, claims 28 and 57 do not include the step of reconstructing a spectrum using a Fourier transform. In all of the cited references, these steps are inherent by the utilization of FTIR spectrometers.

The Examiner combines each of the references Heise, Bhandare, Budinova or Vonach with the '177 Patent, stating:

> Purdy ['177 Patent] provides a solution to the problem by using a chopper for periodically interrupting radiation emitted from the bulb, i.e. modulating intensity of the incident signal: "A method for non-invasive detection of the concentration of an analyte in the blood of a living animal includes the steps of irradiating a body part of the animal with intensity-modulated radiation over a continuous spectrum; detecting the intensity of radiation emitted from the body part at a plurality of discrete wavelength ranges within the continuous spectrum; and using the detected intensity to calculate the concentration of the blood analyte" (col. 2, lines 31-39).

Applicants point out that an element of claim 28 is "passing infrared radiation through the sample and sample container over the pre-defined measurement path to an optical detector, wherein the optical detector measures the intensity of radiation at less than 10 discrete wavelength bands." Furthermore, an element of claim 57 is "wherein the optical sensor uses spectral filtering channels." As previously discussed, Heise, Bhandare, Budinova and Vonach fail to teach these elements. The combination of Purdy's "chopper" still fails to teach these elements. First, the '177 Patent is detecting "emitted" radiation, not transmitted radiation. The Examiner will appreciate that both claim 28 and 57 include elements of "transmitted" radiation. Accordingly, a prima facie case of obviousness has not been established for the amended claims.

Furthermore, the motivation for combining the '177 Patent with Heise, Bhandare, Budinova and Vonach is inappropriately derived by the Examiner. Purdy uses the chopper so that the "living animal" is not burnt during analysis. Both claims 28 and 57 include the element

of "obtaining a sample" and therefore describe invasive analyses. The '177 Patent has introduced the chopper to prevent damage during the "non-invasive" technique. There would be no motivation for combining a chopper meant to prevent burning a living animal to a method which does not involve a living animal, but rather, involves a sample. The lack of relation is evidenced by the fact that the Applicants' specification is completely devoid of any discussion of heating the sample or concern of "overheating of the sensitive biological sample," as stated by the Examiner.

Accordingly, Applicants request that the Examiner withdraw rejections of claims 28 and 57. Claims 29-56 are dependent upon claim 28 and should be withdrawn for at least the reasons discussed in regard to claim 28. Claims 58-69 are dependent upon claim 57 and should be withdrawn for at least the reasons discussed in regard to claim 57.

14. The Examiner has rejected claims 52-55 under 35 U.S.C. 103(a) as being unpatentable over anyone of Heise, Bhandare, Budinova, or Vonach in view of Purdy, as applied to claims 28-51 and 56-69, and further in view of Rule et al. (US 2003/0040683 Al) (Rule).

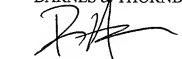
Claims 52-55 directly or indirectly depend from claim 28. As previously discussed, Heise, Bhandare, Budinova, or Vonach in view of Purdy fail to teach or suggest each and every element of claim 28. The combination of Rule with Heise, Bhandare, Budinova, Vonach and Purdy still fails to teach each and every element for at least the reasons stated above. Accordingly, Applicants request that the Examiner withdraw rejections of claims 52-55.

CONCLUSION

Applicant believes that the present application is now in condition for allowance and such action is respectfully requested. If there are any questions or comments that would speed prosecution of this application, the Examiner is invited to call the undersigned at 317-231-7253.

It is respectfully requested that, if necessary to effect a timely response, this paper be considered as a Petition for an Extension of Time sufficient to effect a timely response and that shortages in fees, if any, be charged, or any overpayment in fees credited, to the Account of Barnes & Thornburg, Deposit Account No. 10-0435 with reference to file 3220-73780.

Respectfully submitted,
BARNES & THORNBURG LLP



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